

Non-technical Abstract

A Phase I Study of Vaccination with Autologous, Lethally Irradiated Melanoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor

No consistently effective therapy exists for metastatic melanoma. Interest in the immunotherapy of melanoma has been stimulated by the observation of rare, spontaneous regressions of disease and the increasing evidence that the host can mount an immunologic response against melanoma. We have conducted extensive laboratory studies using a new strategy for inducing anti-tumor immune responses to mouse tumors, including melanoma. By inserting the immunostimulatory gene granulocyte-macrophage colony stimulating factor (GM-CSF) into mouse melanoma tumor cells and injecting them under the skin, systemic anti-tumor immune responses have been induced, resulting in the eradication of implanted tumors at distant sites. Importantly, the tumor vaccine cells could be lethally irradiated after genetic engineering without compromising the efficacy of treatment.

Based on these studies, we have performed during the past two years a Phase I study in patients with metastatic melanoma of vaccination with lethally irradiated, autologous melanoma cell engineered by retroviral mediated gene transfer to secrete GM-CSF. This study has documented the consistent induction of potent anti-tumor immunity (associated with clinical benefit in a significant number of patients) without the development of significant toxicity. Because of the complexity and length of producing vaccines with retroviral vectors, however, the current study will examine the biologic activity of a greatly simplified method for vaccine preparation. In this trial, harvested tumor masses will be prepared to single cell suspension, infected overnight with an adenovirus expressing human GM-CSF, and then irradiated and frozen the following day.

The proposed study seeks to determine the safety and toxicity of administering this type of genetically engineered cancer vaccine. While the study is not intended to assess the efficacy of this treatment, it will provide important information that will be incorporated into future efficacy studies. Measurements will be made in this trial of any immunologic responses stimulated by the vaccine.